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Campthothecin as inhibitor of liprin alpha-2 for management of Breast cancer

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ABSTRACT

Liprin alpha 2 protein which is present in body is responsible for breast cancer by increasing the cell motility of cancerous cells. In earlier studies some fungal pigments are used to inhibit the function of liprin protein and used for curing breast cancer. Now by following the approach of docking an alkaloid (campthothecin) is expected for showing some useful results against this protein. For this we take protein structure from protein data bank and take ligand (campthothecin) from zinc data base. Docking of ligand-protein was done by using Swiss docking and score is checked of this docking result by DSX scoring. The resulting energy of this docking is -7.27 which shows that it has some effective effects against liprin action. These results cleared that this ligand may be expected drug to cure hormone dependent breast cancer.

Keywords: Liprin alpha 2; Campthothecin; Alkaloid; Breast Cancer; DSX Scoring; Docking; Protein Data Bank; Fungal Pigments; Ligand.

1. Introduction

Breast cancer is a type of cancer which produces from cells proliferation or uncontrolled growth of breast cells. Breast cancer commonly begins in the internal lining of mammary ducts or glandular tissues. A malignant cancer can spread from its origin to other body parts. Breast cancer in the glandular tissues is called lobular carcinoma, while in mammary ducts is known as ductal carcinoma. It is the most dangerous cancer in female's around the world [1]. It represents 16% of every female disease and 22.9% of malignant tumor in ladies. Death percentage in males and females from this disease is 18.2% in all over the world [2].

Liprin are well monitored framework proteins that manage all cellular functioning and synape improvement by binding to target proteins. The interaction of liprin and its target is not well known [3]. Its target protein causes the breast cancer due to its ability of increasing the cell motility across the membranes.

The alkaloid "Campthothecin" a strong antineoplastic agent which was isolated in China from Camptotheca acuminata Decaisne (clinically important tree for development of anticancer drugs). In spite of the fact that it's expected use in clinical medicines, the unmodified Campthothecin experiences disadvantages that undermine its applications because of exceptionally low dissolvability in fluid media and high toxicity [4]. Although in earlier studies campthothecin has been studied for their anticancerous effect but another way is used to develop new drug by considering the anticancerous effect of campthothecin against liprin alpha 2 which causes breast cancer. Our review would be advantageous in delivering new lead particles and medication focuses for the management of breast cancer [5].

1.1. Study Objectives

Objectives of the present study were: (1) To express the chemical structure of Camptothecin. (2) To evaluate the drug scoring for Camptothecin. (3) To know the structure of liprin alpha 2 protein. (4) To understand the molecular mechanisms through which Liprin Alpha-2 influences the progression and metastasis of breast cancer. (5) To

evaluate the docking energy for the interaction.

2. Methodology

2.1. Retrieval of target

The target, liprin alpha 2 protein was download from protein data bank. I take its chain A and B for my study.

2.2. Retrieval of ligand

The chemical structure of campthothecin a compound of alkaloid family was obtained from pub Chem database.

2.3. Target and ligand Improvement

For docking examination, PDB directions of the objective protein and ligand particles were enhanced by UCSF chimera software. These directions had least energy as I analyze and had stable compliance.

2.4. *In-Silico* Studies

The dynamic sites are the directions of the ligand in the first objective protein matrices and these dynamic binding destinations of target protein were resolved utilizing the MetaPocket 2.0 virtual software. A computational methodology, ligand-target docking was embraced to explore to examine the liprin alpha 2 as focus with ligand to understand about specific protein target. As a last point, these buildings were exposed to docking by utilizing Swiss dock tool of sub-atomic docking (http://www.swissdock.ch). The energy of connection of ligand with the objective enzyme is portrayed as "matrix point". At each step of excitement, the ligand - protein connection of energy was checked by nuclear partiality possibilities processed on a framework. The leftover boundaries were set as a default.

3. Results

Table 1 is showing the chemical and physical properties of campthothecin which I select as a ligand have molecular weight 348.35204g/mol and its molecular formula is $C_{20}H_{16}N_2O_4$. This ligand has one hydrogen donor and five hydrogen acceptor. This ligand molecule has complexity of 742.

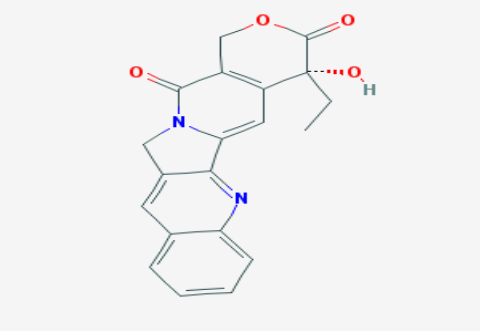

Figure 1. Structure of campthothecin (Source: https://pubchem.ncbi.nlm.nih.gov/compound/Camptothecin)

Table 1. Chemical and physical properties of ligand for their biological activity

Ligand name	Campthothecin
Molecular weight	348.35204g/mole
Molecular formula	$C_{20}H_{16}N_2O_4$

X logP3	1
Hydrogen donor	1
Hydrogen acceptor	5
Complexity	742

Table 2. Scoring of selected ligand with targeted protein

Ligand	RMSD	Rank (score)	Score
Campthothecin	none	1	15

Table 2 shows the DSX scoring results which provide that campthothecin has none rmsd value and its rank score is one and score is fifteen. Its fifteen score shows that this ligand-protein interaction have great stability and scoring is a process of evaluating the quantity of great intermolecular collaboration, for example, hydrogen holding or hydrophobic interaction.

Table 3. Energy and full fitness numberings during docking of ligand particles and liprin alpha as target

Ligand name	Show	Cluster	Maximum fitness (kcal/mol)	Approximated ΔG (kcal/mol)
Campthothecin	0	0	-1874.59	-7.27
Campthothecin	1	0	-1872.37	-6.67
Campthothecin	2	0	-1871.57	-6.93
Campthothecin	3	0	-1871.47	-6.80

Table 3 shows the energy and full fitness values obtained during docking analysis. Here the full fitness value of ligand is -1874.59 kcal/mol and estimated energy in kcal/mol is -7.27 when cluster and show both are zero. This table shows that when show increases its estimated energy value.

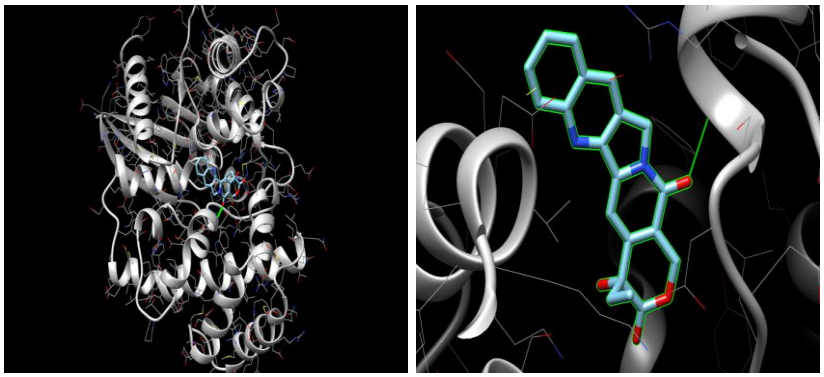

Figure 2. Molecular docking of ligand with protein

The result of liprin-campthothecin docking was relieved that computational drug designing is possible of these two because its docking results shows stability due to the formation of hydrogen bond and other hydrophobic interactions of ligand with target protein (Figure 2) and the final docking energy for campthothecin was observed is -7.27 which shows its potency for effective drug (Table 3). The ligand molecule (campthothecin) showed significant interaction with the target protein based on RMSD value which obtained as a result of DSX scoring

(Table 2). In conclusion, molecular docking result of ligand-protein revealed that these compounds dock well and campthothecin have effective results against liprin alpha 2 functions and to cure the breast cancer.

4. Discussion

In structural molecular biology and computer assisted drug development "molecular docking" is utilized as key tool in order to anticipate the proclivity and action of the small particle. Docking is regularly utilized to divine the limiting direction of small particle drug possibility to their protein targets. Subsequently docking key assumes a significant part in the normal plan of new medicine. The objective of ligand-protein docking is to decide the limiting methods of ligand with the protein [3]. Therefore, biologically active alkaloids provided best perceptive of the drug receptor interaction as a result of molecular docking studies [6].

5. Conclusion & Future Suggestions

The present results showed that the ligand used may be an expected drug to cure hormone dependent breast cancer. The future suggestions for the current study could focus on several aspects for future research and development:

- Conduct further studies to explore the precise molecular mechanisms by which camptothecin inhibits Liprin Alpha-2.
- Explore the synergistic effects of camptothecin and other targeted therapies (e.g., HER2 inhibitors, PI3K inhibitors) in breast cancer models.
- Investigate how the bioavailability of camptothecin can be enhanced through novel delivery methods (e.g., nanoparticles, liposomes)
- Investigate the long-term toxicities associated with camptothecin treatment.

Declarations

Source of Funding

This study did not receive any grant from funding agencies in the public, commercial, or not–for–profit sectors.

Competing Interests Statement

The authors declare no competing financial, professional, or personal interests.

Consent for publication

The authors declare that they consented to the publication of this study.

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